Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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PII: S0002-8177(21)00786-8

DOI: https://doi.org/10.1016/j.adaj.2021.12.007

Reference: ADAJ 2201

To appear in: *The Journal of the American Dental Association*

Received Date: 13 October 2021

Revised Date: 17 December 2021

Accepted Date: 26 December 2021

Please cite this article as: Silva A, Azevedo M, Sampaio-Maia B, Sousa-Pinto B, The effect of mouthwashes on SARS-CoV-2 viral load: a systematic review, *The Journal of the American Dental Association* (2022), doi: https://doi.org/10.1016/j.adaj.2021.12.007.

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No author has conflict of interest regarding the authorship and/or publication of this article.

Acknowledgments

This work is a result of the project POCI-01-0145-FEDER-029777, co-financed by Competitiveness and Internationalisation Operational Programme (POCI), under the PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund (ERDF) and through national funds by the FCT – Fundação para a Ciência e a Tecnologia. Maria João Azevedo PhD fellowship was supported by FCT/MCTES scholarship (SFRH/BD/144982/2019).

PROSPERO website registration: CRD42021237418

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ABSTRACT

Background: Considering the oral cavity a major entryway and reservoir for SARS-CoV-2, the aim of this study was to perform a systematic review of *in vivo* and *in vitro* studies to assess the effectiveness of mouthwashes on SARS-CoV-2 viral load.

Types of study: We searched PubMed, Web of Science, Scopus, MedRxiv, and bioRxiv databases, including *in vitro* and *in vivo* studies assessing the virucidal effect of mouthwashes on SARS-CoV-2 or surrogates. From a total of 1622 articles retrieved, 39 were included in this systematic review.

Results: Povidone-iodine (PVP-I) was the most studied mouthwash (14 *in vitro* and 9 *in vivo* studies), frequently showing significant reductions in viral load *in vitro* assays. Similarly, cetylpyridinium chloride (CPC) also showed good results, although evaluated in fewer studies. Chlorhexidine gluconate (CHX) and hydrogen peroxide (H_2O_2) showed conflicting results on SARS-CoV-2 load reduction in both *in vitro* and *in vivo* studies.

Practical implications: PVP-I-based mouthwashes appear to be the best option as an oral pre-rinse in dental context for SARS-CoV-2 viral load reduction. Although the results of primary studies are relevant, there is a need for more *in vivo* studies on mouthwashes, in particular randomized controlled clinical trials, to better understand their effect on SARS-CoV-2 viral load and infection prevention.

Key-Words: Saliva, COVID-19, Decision-making, Microbiology, Public Health, Infection Control

INTRODUCTION

SARS-CoV-2 is a beta-coronavirus. Beyond the recent SARS-CoV-2 outbreak, beta-coronavirus were associated with two other outbreaks, namely severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)[1,2].

Binding of SARS-CoV-2 to human cells mainly occurs via the angiotensin-converting enzyme 2 (ACE2) receptor[3,4], highly expressed in the oral cavity, mainly in the epithelium of the tongue, but also in gingival tissue, particularly on the buccal surface of the sulcular epithelium. Considering the oral cavity may represent a major entryway and a reservoir of SARS-CoV-2[5-7], the scientific community adjusted disinfection protocols and preprocedural protocols for dental practice. Widespread use of protective suits was advised, and use of goggles and shoe covers was reinforced, as well as stricter patient triage ahead of the appointment[8].

Preprocedural gargling with a mouthwash was hypothesized to possibly act as an additional protective measure, reducing the oral load of SARS-CoV-2[9]. Even before the COVID-19 pandemic, preprocedural gargling was used in dentistry to reduce microbial load before surgeries or routine procedures[9]. Currently, there are published guidelines advising the use of some mouthwashes aiming to reduce SARS-CoV-2 salivary viral load prior to dental appointments, in particular de use of H_2O_2 mouthwashes[10-14]. However,supporting evidence on mouthwashes effectiveness on SARS-CoV-2 viral load is still scarce, with no systematic reviews analysing the evidence from both *in vitro* and *in vivo* studies on this question[15,16] Thus, this study aimed to assess the effectiveness of mouthwashes in reducing SARS-CoV-2 viral load.

METHODS

Protocol and registration

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist and is registered on PROSPERO website.

Eligibility criteria

Inclusion criteria: *In vitro* and *in vivo* studies assessing the virucidal effect of mouthwashes on SARS-CoV-2 or surrogates. Exclusion criteria: Reviews, letters to the editor, personal opinions, product news, book chapters, case reports, congress abstracts, protocol suggestions, editorials, correspondence articles, recommendations, trial designs, hypotheses, and studies with animals.

Information sources and search strategy

To develop this review, searches were performed in MEDLINE (via PubMed), Scopus, and Web of Science databases. Searches were conducted on January 13th, 2021, with an update on November 23rd, 2021. This search was complemented with a manual search on MedRxiv and bioRxiv preprint databases. Full query is described in **Table 1**. Since the first scientific publications on SARS-CoV-2 concern the year 2020, we limited the search to articles published in 2020 and 2021.

Study selection

After removing duplicates, the titles and abstracts of retrieved publications were independently reviewed by two reviewers. Studies not excluded in the screening phase were fully read, with full-text analysis being independently performed also by two investigators. Any divergence was solved by a discussion with a third reviewer.

Data extraction

Data was independently extracted by two reviewers using a purposely built online form. In case of any inconsistency of data collection, a third author resolved it through discussion. The following variables were retrieved from each primary study: author, title, year, country, type of study, sample number and type, patient characterization, intervention and control group, virus strain, type of mouthwash, concentration, number of mouthwashes per day, rinsing duration, treatment duration, and decrease in viral load. For *in vitro* studies, the cell lineage used, and existence of interfering substances were also assessed.

Risk of bias in individual studies

Assessment of the risk of bias (RoB) of included randomized controlled trials (RCT) was carried out independently by two reviewers according to Cochrane Collaboration tool for assessing RoB[17]. Disagreements between reviewers were resolved after

discussion and analysis. No RoB assessment was performed on *in vitro* studies or observational before-after studies due to a lack of consensually accepted tools for assessing RoB in those specific studies.

Summary measures

We considered all outcome measures directly evaluating SARS-CoV-2 viral load. Main outcome measures presented in this systematic review are viral load expressed in logarithmic (log) reduction value, copies per milliliter (copies/mL), and Relative Light Units (RLU). When primary studies used a mouthwash with known concentration and presented the viral load decrease in logarithmic scale, such results were interpreted following the European Norm EN-14476, which recognizes antiseptics virucidal capacity when achieving a reduction on viral load equal or greater than 4 $\log_{10}$[18]. Therefore, results of the primary *in vitro* studies when expressed in log scale were classified according to three levels considering virucidal activity (viral load reduction): high efficacy (≥4 $\log_{10}$; +); moderate efficacy (≥3 $\log_{10}$ and <4 $\log_{10}$; ±); and low efficacy (<3 $\log_{10}$; -). To simplify the comparison between studies results expressed in Molar were converted to a percentage (%, in g/100mL). Results presented as a percentage of inactivation or fold reduction were converted to a logarithmic scale.

Synthesis of results

Due to methodological diversity of included primary studies, it was not possible to carry out a meta-analysis.

RESULTS

Study selection

A total of 1560 articles were retrieved from bibliographic databases (MEDLINE, Scopus, and Web of Science), and 62 from preprint databases. The study selection process is described in **Figure 1**.

Study characteristics

From a total of thirty-nine included studies, thirty-three had been published as peer-reviewed articles and six were preprints (**Appendix Table 1)**. Twenty-four of the published articles were performed *in vitro* and ten were *in vivo,* five of which were RCT while the remaining were uncontrolled before-and-after studies. Five of the included preprints were performed *in vitro* and one was *in vivo*.

In vivo studies included COVID-19 positive hospitalized patients[19-27], and home-isolated patients[22,28]. All *in vivo* studies quantified SARS-CoV-2 viral load via Polymerase Chain Reaction (PCR), targeting genes E[19-22,24], RNA-dependent RNA polymerase (RdRP)[20,22,24], nucleo-capsid (N)[22-24,26,27], S and R [23]. Three *in vivo* studies used water as a control[21,24,27], one used RNA from trizol-inactivated virus[26]. One used a similar solution regarding aspect and content but without virucidal components[28]. *In vivo* studies evaluated the reduction of SARS-CoV-2 in viral titers: four presented the results with cycle threshold (Ct) fold changes[21,23,24,27], three in the form of a logarithmic reduction value[20,22,25], one in the form of a logarithmic reduction percentage scale[28], one in a percentage scale[26], and one in copies per milliliter[19].

Regarding SARS-CoV-2 strains used across *in vitro* studies, several used well-characterized strains, being the most used USA-WA1/2020[29-37]. Four studies used a SARS-CoV-2 strain directly obtained from an infected patient[38-41], while one study did not report the strain employed[42]. *In vitro* studies were performed under dirty[43-47], clean[29,31-35,37-39,41,42,48-54], or both conditions[36,40,55,56], being these terms referring to the existence of interfering substances. Two *in vitro* studies did not provide information about the existence of interfering substances[30,57].

In vivo and *in vitro* studies applied the intervention solution for a pre-determined period – mouthwash contact time, most commonly ranging from 15 to 120 seconds. Seven *in vitro* studies included periods of application of 5 minutes or more[30,34,41,42,51,53,57].

Risk of bias within studies

Two RCT were marked as a high RoB study[21,27], while the other three were marked as low RoB studies[24,26,28] (**Appendix Table 2**). The other five *in vivo* studies were "uncontrolled before-after" studies including a low number of participants and for which the assessment of RoB was not feasible.

Results of individual studies

Five *in vivo* studies showed the virucidal efficacy of PVP-I solutions on SARS-CoV-2 **(Appendix Table 3).** Seneviratne*, et al.* [21] conducted a RCT and reported a 30-second rinse with 0.5% PVP-I conducted on a group of four hospitalized patients resulted in a significant reduction of viral load 6 hours post-rinse when compared to water. However, no significant differences were found 5 minutes and 3 hours after rinsing. After using the same concentration of PVP-I, but by performing two consecutive 30-second rinses, Chaudhary*, et al.*[26] verified a 61% reduction on viral load after 15 minutes and a 97% reduction after 30 minutes. The RCT conducted by Elzein*, et al.*[24] found a significant mean Ct difference increase between the paired samples before and after a 30-second 1% PVP-I rinse. In an uncontrolled before-after clinical study, Lamas*, et al.*[22] reported a 60-second 1% PVP-I rinse led to a significant drop (≈5 $\log_{10}$) in viral load in one of the four patients evaluated, sustained for at least three hours. Jayaraman*, et al.*[25] found 1% PVP-I could reduce viral load in saliva up to 1.8±1.1 $\log_{10}$. Significant reductions were observed after 20 and 60 minutes.

In vitro studies demonstrated PVP-I-containing mouthwashes have a virucidal effect on SARS-CoV-2 **(Appendix Table 4)**. **Table 2** summarizes the results found in different studies with application times up to 60 seconds and interpreted following the EN-14476. Concentrations up to 0.75% showed moderate-to-high efficacy in reducing SARS-CoV-2 viral load[29,31-33,44,49,52,53,55]. The 60-second application of PVP-I with concentrations between 0.5% and 0.58% presented high efficacy results in the 4 studies evaluating this condition[31,49,53,55]. Concentrations of PVP-I between 1.25% and 2.5% consistently showed moderate-to-high efficacy results[29,31-33]. Applying concentrations of PVP-I greater than 2.5% showed low[46] (PVP-I 7.5%), moderate[43,53] (PVP-I 5% and 7.5%), and high efficacy[44,53] (PVP-I at 7.5% and 10%) within 15 to 30 seconds. The 60-second application also reached moderate-to-high efficacy results (PVP-I concentrations ranging from 5% to 10%)[43,53].

Regarding H_2O_2, Gottsauner*, et al.*[19] conducted an *in vivo* study assessing virucidal efficacy of a 30-second H_2O_2 (1%) rinse with. No significant difference was found between baseline and the viral load 30 minutes after rinsing. Chaudhary*, et al.*[26] found that two consecutive 30-second H_2O_2 (1%), led to a 90% reduction after 15 and 30 minutes. Jayaraman*, et al.*[25] reported a 30-second H_2O_2 (1.5%) rinse could decrease the viral load up to 1.6±1.5 $\log_{10}$ after 60 minutes. A 60-second H_2O_2 (1.5%) rinse led to a significant reduction on viral load immediately after and 30 minutes after rinsing,

but not after 60 minutes[27]. *In vitro* studies on the virucidal effect of H_2O_2 showed very limited success **(Table 3 and Appendix Table 4)**.

Chlorhexidine gluconate mouthwashes virucidal efficacy was evaluated with *in vivo* and *in vitro* studies (**Appendix Tables 3 and 4)**. In an RCT, Seneviratne*, et al.*[21] studied the effect of CHX mouthwashes in a group of six patients and found no reduction of viral load. Another RCT by Elzein*, et al.*[24] reported a mean Ct increase of 5.7 after a 30-second CHX (0.2%) rinse. Eduardo*, et al.*[27] performed a RCT which studied the effect of a 30second CHX (0.12%) rinse and found a significant reduction on viral load 60 minutes after rinsing. On other RCT, Chaudhary*, et al.*[26] reported CHX (0.12%) achieved a 90% decrease on viral load 15 minutes after the two consecutive 30-second rinses, but only a 70% decrease after 30 minutes. Yoon*, et al.*[20] performed an uncontrolled before-after clinical study on the effect of a 30-second CHX (0.12%) rinse on two hospitalized patients. The authors observed a transient decrease in viral load for two hours after rinsing.. In one patient, one-hour post rinse, no decrease on viral load was observed. Jayaraman*, et al.*[25] also reported a limited decrease in viral load on salivaafter 90 minutes. Considering application times of up to 60 seconds **(Table 3)**, *in vitro* application of CHX with concentrations lower than 0.16%) showed low efficacy within 15, 30, and 60 seconds[42]. However, one author reported moderate efficacy within 30 seconds [39] and other reported high efficacy after 30 and 60 seconds[40]. The use of 0.2% CHX also showed low efficacy after 30 seconds[45] and 60 seconds[49]. One preprint article showed CHX (0.12%) achieved low, moderate, and high efficacy, depending on the viral strain used[36]. Meister*, et al.*[45] reported low efficacy results after a 30-second rinse with a CHX mouthwash with unknown concentration.

Cetylpyridinium chloride *in vivo* virucidal activity was studied in a RCT by Seneviratne*, et al.*[21] on a group of four hospitalized patients **(Appendix Table 3)**. CPC 0.075% mouthwash significantly reduced viral load within 5 minutes of use. Compared to the control group, the viral load reduction with CPC was maintained for 3 and 6 hours. *In vitro* studies demonstrated CPC-containing mouthwashes have a virucidal effect on SARS-CoV-2 **(Appendix Table 4)**. Considering application times between 30 and 60 seconds **(Table 3)**, concentrations of up to 0.3% showed low-to-high efficacy[43,46,48,50,54,56]. The 20 second application of CPC had moderate-to-high efficacy[54]. Meyers*, et al.*[43] reported a 120-second application of 0.07% CPC showed

moderate-to-high efficacy. Muñoz-Basagoiti*, et al.*[38] reported moderate results with a 120-second application of CPC at a concentration of up to 10mM (0.3%).

Other mouthwashes, either more complex or with less frequently used active compounds, were studied *in vivo* and *in vitro* by several authors **(Appendix Tables 3** and **4)**. Carrouel*, et al.*[28] studied the effect of a 60-second CDCM rinse, a Citrox, and ß-cyclodextrin containing mouthwash. This study reported a significant decrease in viral load of approximately 13% when using the mouthwash, compared to a 7% decrease observed in the placebo group. Eduardo*, et al.*[27] conducted a RCT studying the effect of performing a 60-second H_2O_2 (1.5%) (Peroxyl®), combined with a 30-second CHX (0.12%) (PerioGard®) rinse. This combined rinse only achieved minor in Ct values when compared to the placebo group. However, when rinsing with a mouthwash containing CPC (0.075%) and Zinc Lactate (0.28%) a significant decrease in salivary viral load was achieved for up to 60 minutes. On an uncontrolled before-after study, Schürmann*, et al.*[23] studied the effect of a 60-second Linola® sept rinse and reported a mean value increase of Ct values of 3.1 (basal versus after-rinsing).

In vitro studies included a diversity of complex mouthwashes. Listerine® mouthwashes were studied by several authors, although each formulation was only assessed in one study, apart from Listerine® Cool Mint® that was assessed by two studies. Listerine® mouthwashes showed variable efficacy[43,45,46,49] **(Table 4)**.

DISCUSSION

Summary of evidence

In this systematic review, we included primary studies assessing the virucidal effect of mouthwashes regarding SARS-CoV-2, that presented a diverse set of methodologies and assess a wide range of mouthwashes. PVP-I was most frequently studied mouthwash, with most *in vitro* studies showing some promising results. The results of *in vivo* studies also pointed to a positive effect of PVP-I on oral viral load reduction, although limitations were found in their methodologies. Similarly, CPC showed positive preliminary results. The use of H_2O_2 and CHX showed conflicting results on SARS-CoV-2 load reduction in both *in vitro* and *in vivo* studies.

To the best of our knowledge, this is the first systematic review analyzing information both from *in vivo* and *in vitro* studies. A previous systematic review had assessed *in vitro* studies, with results consistent to those displayed in this study[15].

Considering mouthwashes as antiseptics, they should follow regulating norms. The International Organization for Standardization (ISO) defines on ISO-16408:2015 the chemical and physical properties of oral rinses, as well as of their test methods, but guidelines for microbiological analysis are specific to mold, bacteria, and yeast, lacking virus instructions[58]. There seems to be a lack of standardization on the evaluation of mouthwashes regarding virucidal properties. According to the European Standard EN-14476, an antiseptic is effective when it reduces viral load ≥4 $\log_{10}$[18]. Although EN-14476 is not specific towards oral rinses, due to the lack of more appropriate regulation, we decided to compare our results in light of this European Norm for assessing mouthwash virucidal properties.

Included primary studies displayed substantial diversity in their methodologies and results presentation, limiting our capacity of comparing different mouthwashes. PVP-I-based mouthwashes appear to have potential for reducing SARS-CoV-2 in the oral cavity. Nonetheless, these results must be cautiously interpreted. The RCT conducted by Elzein*, et al.*[24] has a low RoB and reported a significant decrease in viral load post mouthwash. However, neither the RCT conducted by Seneviratne*, et al.*[21], which had a high RoB and just 16 patients, nor the RCT conducted by Chaudhary*, et al.*[26] revealed such a significant decrease. Jayaraman*, et al.*[25] did not find a significant decrease in an uncontrolled before-and-after study. It also does not seem to exist a dose-response relationship (i.e., studies assessing the effect of higher PVP-I concentrations on SARS-CoV-2 viral load do not appear to obtain better results) or a time-response relationship.

The use of CPC mouthwashes for reducing the viral load also showed encouraging results. Of note, CPC is also capable of inactivating *influenza* viruses both *in vitro* and *in vivo*, but only after 10 minutes of contact time[59].

In the included primary studies, H_2O_2 and CHX-based mouthwashes produced a varied effect on SARS-CoV-2 viral load. As their effect was inconclusive, recommending their use may not be adequate. CHX and H_2O_2 are already currently used in some oral care products, with CHX displaying broad-spectrum antimicrobial

activity[60], including against anaerobic oral bacteria[61]. Worldwide government agencies and professional associations currently advise the use of pre-procedural rinse with H_2O_2 mouthwashes to reduce oral SARS-CoV-2 viral load mouthwashes[10-14], so there may be a need to reconsider these directives.

Some complex mouthwashes like Listerine® Total Care, Listerine® Advanced, and Listerine® Antiseptic showed promising results in reducing SARS-CoV-2 viral load in the oral cavity, although they were evaluated by only one or two studies each. Using these mouthwashes as a coadjutant in oral health is well established, contributing to the reduction of dental biofilm and gingivitis[62].

The included primary studies have the limitation of only evaluating the presence of viral particles and not their viability or infectious capacity, therefore using other techniques as viability-PCR could be employed to study the infectious potential of the virus. The United States Environmental Protection Agency, the Centers for Disease Control and Prevention, and the Lawrence Livermore National Laboratory are currently developing a Rapid Viability-Reverse Transcription PCR to evaluate SARS-CoV-2 viability on surfaces and objects[63]. Analyzing aerosols could be also a realistic way to study the impact of dental procedures on the dissemination of viral particles. Choi*, et al.*[64] performed a study on aerosol sampling in the emergency department of a university hospital, collecting a total of forty-four samples, twelve of which were positive to known respiratory viruses - influenza A, influenza D, and adenovirus. Lednicky*, et al.*[65] demonstrated the generation of aerosols containing SARS-CoV-2 virions by patients with COVID-19 respiratory manifestations even in absence of aerosol-generating procedures, which can lead to virus transmission. The authors were also able to quantify the generated viral particles detected from a distance higher or equal to two meters. These results highlight the importance of preventive measures such as pre-rinse antiseptic mouthwash but also a rubber dam isolation given that both strategies can significantly reduce aerosol pathogen load[65,66].

In addition to the wide diversity of study methodologies, and of results presentations, a major limitation of this systematic review is the scarcity of RCTs, with only five meeting eligibility criteria[21,24,26-28]. The validity of the conclusions is affected by the bias of the included primary studies, in this case, regarding the high RoB of two of the RCT. Besides, the other five *in vivo* studies have important limitations in their designs,

including the absence of randomization or even a control group, and a relatively low number of included patients; this prompts a low level of evidence and hampers the precision of their estimates, respectively. Although *in vitro* studies are part of the tests proposed by EN-14476[18], their results cannot be directly transposed to *in vivo* application of these mouthwashes. *In vivo* studies should be RCT conducted with a better study design, including a higher number of patients, include a control solution, and express their results as virus log reduction allowing a better interpretation of results with a greater level of evidence.

A recurrent inadequacy found in selected studies was the existence of studies that include times of application not feasible in clinical practice. Some *in vitro* studies had application times of 30 minutes[30], and one preprint article also considered an application with a duration of 72 hours[51]. We find these application times unrealistic and not adequate for clinical practice since patients are normally only able to gargle for a short period[67], usually up to 60 seconds.

Suggestions for Future Studies

There is a need for more *in vivo* and *in vitro* studies on different mouthwashes that consider adequate and realistic application times, of up to 60 seconds. Well-designed RCT with a larger number of patients should be considered a priority when it comes to design of *in vivo* studies. Based on results from already published primary studies, future studies should mainly focus on PVP-I and CPC-based mouthwashes. Furthermore, the studies should present their results in form of a logarithmic reduction that can be compared according to EN-14476. Studying mouthwash-induced cytotoxicity should be a concern when assessing virucidal properties of different mouthwashes with different concentrations. Studying viral viability post-rinse and viral presence in aerosols should be considered to better assess the real impact of virus dissemination in the dental setting. Overall, guidelines for the standardized evaluation of the effect of mouthwashes on viruses are needed.

Conclusions

In conclusion, considering the current knowledge, using PVP-I-based solutions as a preprocedural rinse in dental setting appears to be potentially effective in reducing SARS-CoV-2 oral load. There are no powerful arguments to consider using of H_2O_2 and CHX effective regarding SARS-CoV-2 virus and their use as a pre-procedural

mouthwash aiming to reduce SARS-CoV-2 oral load should be revised. More RCTs together with *in vitro* studies are urgent to further evaluate PVP-I and CPC-based mouthwashes and test other commercially available mouthwashes showing potential results on SARS-CoV-2 load reduction.

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Figure Legend

Figure 1. PRISMA study selection flowchart

Tables and legends

Table 1. Database search strategy.

Table 1. PVP-I in vitro effect on SARS-CoV-2 oral viral load. Results interpretation accordingly to EN-14476, considering a reduction on viral load greater or equal than 4 log10 as a high efficacy (⊕), a reduction greater than 3 log10 and lower than 4 log10 as a moderate efficacy (±), and a reduction lower than 3 log10 as a low efficacy (⊖).

Table 2. H_2O_2, CHX, and CPC mouthwashes in vitro effect on SARS-CoV-2 oral viral load. Results interpretation accordingly to EN-14476, considering a reduction on viral load greater or equal than 4 log10 as a high efficacy (⊕), a reduction greater than 3 log10 and lower than 4 log10 as a moderate efficacy (±), and a reduction lower than 3 log10 as a low efficacy (⊖).

Table 3. Other mouthwashes in vitro effect on SARS-CoV-2 oral viral load. Results interpretation accordingly to EN-14476, considering a reduction on viral load greater or equal than 4 log_{10} as a high efficacy (⊕), a reduction greater than 3 log_{10} and lower than 4 log_{10} as a moderate efficacy (±), and a reduction lower than 3 log_{10} as a low efficacy (⊖).

Appendix

Title: The effect of mouthwashes on SARS-CoV-2 viral load: a systematic review

Appendix Table 1. Studies characterization.

		In vitro	*In vivo*	
			Randomized controlled trials	Uncontrolled before-and-after studies
Peer-reviewed	Anderson, *et al*. [44]	x		
	Bidra, *et al.* [29]	x		
	Bidra, *et al*. [33]	x		
	Carrouel, *et al*. [28]		x	
	Frank, *et al*. [32]	x		
	Gottsauner, *et al*. [19]			x
	Hassandarvish, *et al*. [55]	x		
	Jain, *et al*. [39]	x		
	Koch-Heier, *et al*. [50]	x		
	Lamas, *et al*. [22]			x
	Meister, *et al*. [45]	x		
	Meyers, *et al*. [43]	x		
	Pelletier, *et al*. [31]	x		
	Schürmann, *et al*. [23]			x
	Seneviratne, *et al*. [21]		x	
	Xu, *et al*. [30]	x		
	Yoon, *et al*. [20]			x
	Almanza-Reyes, *et al*. [51]	x		
	Davies, *et al*. [49]	x		
	Elzein, *et al*. [24]		x	
	Muñoz-Basagoiti, *et al*. [56]	x		
	Steinhauer, *et al*. [42]	x		
	Zoltán [35]	x		
	Santos, *et al*. [41]	x		
	Shewale, *et al*. [37]	x		
	Shet, *et al*. [53]	x		
	Kariwa, *et al*. [52]	x		
	Tiong, *et al*. [40]	x		
	Meister, *et al*. [47]	x		
	Komine, *et al*. [54]	x		
	Santos, *et al*. [57]	x		
	Chaudhary, *et al*. [26]		x	
	Eduardo, *et al*. [27]		x	
Pre-print	Green, *et al*. [48]	x		
	Jayaraman, *et al*. [25]			x
	Mantlo, *et al*. [34]	x		
	Muñoz-Basagoiti, *et al*. [38]	x		
	Statkute, *et al*. [46]	x		
	Anderson, *et al*. [36]	x		

Appendix Table 2: Risk of Bias assessment.

	1.1 Random sequence generation	1.2 Allocation concealment	2.1 Selective reporting	3.1 Other sources of bias	4.1 Blinding (participants and personnel)	5.1 Blinding (outcome assessment)	6.1 Incomplete outcome data
Senevirat ne, *et al*. [21]	⊕	⊕	⊕	?	⊕	⊖	⊕
Carrouel, *et al*. [28]	⊕	⊕	⊕	⊕	⊕	⊕	?
Elzein, *et al*. [24]	?	⊕	⊕	?	⊕	⊕	⊕
Chaudhar y, *et al*. [26]	?	⊕	?	?	⊕	⊕	?
Eduardo, *et al*. [27]	⊕	⊕	⊕	⊕	⊖	⊕	⊕

⊕ Low Risk of Bias; ? Unclear Risk of Bias; ⊖ High Risk of Bias.

Appendix Table 3: *In vivo* efficacy of different mouthwashes on SARS-CoV-2 viral load.

Publication	Study design	Setting	Number of included participants	Assessment of viral load	Product, duration of rinse	Comparison	Results
Seneviratne, *et al*. [21]	RCT	Hospitalized patients with a nasal swab and saliva RT-PCR positive for SARS-CoV-2. Mean age per group±SD: PVP-I (n=4): 40.7±11.5; CHX (n=6): 43.6±8.6; CPC (n = 4): 35.7±8.5; Water (n = 2): 36±14.1 Single rinse performed in a single day.	16	Saliva (passive drool), via RT-PCR	PVP-I (0.5%), 30s CHX (0.2%), 30s CPC (0.075%), 30s	Water	Ct values detected in all 16 patients were within the range of 15.6–34.5, with a mean value of 27.7±4.8; Results are presented in form of fold change calculated as a ratio between Ct value at different timepoints and Ct value at baseline. PVP-I: significant increase in fold change was obtained only at 6h (*ratio*=1) post-rinsing with PVP-I in comparison with water ($p<0.01$). In comparison to the water group, the PVP-I group patients had higher fold increases in Ct value after 5min (*ratio*=1.1) and 3h (*ratio*=1.2) of post-rinsing, but no significance was achieved. CHX: patients demonstrated a varied effect among saliva Ct values after 5min rinsing and hence further studies with a larger sample size are required to determine its significance. CPC: significant increase in fold change of Ct value at 5min (*ratio*=1) and 6h (*ratio*=0.9) was observed post-rinsing with CPC mouth-rinse compared to the water group patients ($p<0.05$). Although the fold changes in Ct values were higher at 3h (*ratio*=0.9) in the CPC group, no significance was achieved ($p=0.20$).
Carrouel, *et al*. [28]	RCT	Home-isolated patients diagnosed with COVID-19. Mean age per group±SD: Placebo (n=88): 44.08±16.16 CDCM (n=88): 42.06±14.97	176	Saliva (method not specified), via (rt)RT-PCR	CDCM: ß-cyclodextrin (0.1%) and citrox(0.1%), 60s	Similar appearance and content solution without antiviral components	Day one: A significant difference was observed in viral load reduction in the before-after comparison of the same patients receiving CDCM versus no difference for the placebo group from T1 (first sample other than basal on day one) to T2 (Second sample other than basal on day one) ($p=0.036$). The percentage median decrease

Publication	Study design	Setting	Number of included participants	Assessment of viral load	Product, duration of rinse	Comparison	Results
		Three rinses per day, for 7 days.					(log10 copies/mL) was -12.6% [-29.6% - -0.2%] (CDCM) versus -6.7% [-21.2% - 10.4%] (placebo). At T3 (third sample other than basal on day one), the salivary viral load decreases were significant for both groups compared to T1 (CDCM: p<0.001; placebo: p=0.002) but with no significant difference between the 2 groups. Seven days: continuous decrease for the CDCM group and the placebo group was observed for 7 days. On day 7, no significant difference between patients receiving CDCM and those receiving placebo (p=0.388). In both groups, the viral load was significantly lower on day 7 than on day 1 T1 (p< 0.001)
Elzein, *et al*. [24]	RCT	Hospitalized patients diagnosed with COVID-19. Mean age per group±SD: PVP-I group (n=27): 39.9±14.2; CHX group (n=25) 47±15.4; Distilled water group (control) (n=9) 57.2±22.5 Single rinse performed in a single day.	61	Saliva (Passive drool), via rRT-PCR	PVP-I (1%), 30s CHX (0.2%), 30s	Water	Baseline: mean Ct value of human RNaseP in saliva samples before mouthwash was 25.4±2.5[18.4–32.2]; 5 min after for CHX and PVP-I: mean Ct value of human RNaseP in saliva samples after mouthwash was 26±2.7[19.4-32.5]. No significant difference was found between the mean Ct values of human RNaseP in the 2 groups (p=0.332). PVP-I: significant mean difference between the paired samples before (29.9±6.2; median 30.8) and after mouthwash (34.4±6.3; median 34.2) with 1% Povidone-iodine (p<0.0001). CHX: higher significant difference of means was found in paired samples using Chlorhexidine 0.2% (p<0.0001). The mean Ct increased 5.7 after mouthwash. The mean Ct of pre and post mouthwash was respectively 27.7±7.2 (median 27.1) and 33.9±7.1 (median 33.1)

Publication	Study design	Setting	Number of included participants	Assessment of viral load	Product, duration of rinse	Comparison	Results
Chaudhary, *et al*. [26]	RCT	Hospitalized symptomatic adults (aged 21 through 80) diagnosed with COVID-19 via PCR. Age - Median (Range): 64 (25-82) Each mouthwash group was constituted by 10 individuals. Two consecutive rinses on a single day.	40	Saliva (Passive drool), via PCR	PVP-I (0.5%), 30s+30s H_2O_2 (1%), 30s+30s CHX (0.12%), 30s+30s Normal saline, 30s+30s	RNA from trizol-inactivated virus as positive control	After 15 min, CHX (0.12%), H_2O_2 (1%), and normal saline reduced viral load by 90%. On the other hand, PVP-I (0.5%) only reduced the viral load by approximately 61% 15 min after the rinse. After 30 minutes, H_2O_2 (1%) and normal saline reduced the viral load by approximately 90%, while CHX (0.12%) led to an approximately 70% reduction. However, PVP-I (0.5%) led to a 97% reduction on viral load 30 minutes after the rinse.
Eduardo, *et al*. [27]	RCT	Hospitalized (for up to 3 days) adults (aged 18 through 80), previously diagnosed with COVID-19 via nasal swab qRT-PCR with mild-to-moderate symptoms. Median (range) age per group: Placebo group (n=9): 59 (36–85); CPC+Zn (n=7): 46 (34–88) H_2O_2 (n=7): 62 (40–87) CHX (n=8): 53.5 (49–88) H_2O_2+CHX (n=12): 53 (40–72) Single rinse performed in a single day. The H_2O_2+CHX group performed two consecutive rinses, with different gargling times.	43	Saliva (Passive drool), via PCR	0.075% CPC (0.075%) + Zinc Lactate (Zn) (0.28%) mouthwash (Colgate Total 12®), 30s H_2O_2 (1.5%) (Peroxyl®), 60s CHX (0.12%) (PerioGard®), 30s H_2O_2 (1.5%) (Peroxyl®), 60s+ CHX (0.12%) (PerioGard®), 30s	Distilled water	Significant difference in the mean Ct value was observed for CPC+Zn (20.4±3.7-fold reduction), H_2O_2 (15.8 ±0.08-fold reduction) and H_2O_2+CHX (2.1±0.5-fold reduction) immediately after the rinse (T1), when compared to baseline. 30 min after rinsing (T2), H_2O_2 had a significant reduction in viral load (6.5± 3.4-fold reduction). CPC+Zn had a significant reduction up to 60 min (T3) after the rinsing (6.5±3.4-fold reduction), which was not observed after rinsing with H_2O_2 (0.3± 1.3-fold reduction). CHX achieved a >2-fold reduction (T1: 2.1±1.5 fold, T2: 6.2±3.8 fold, and T3: 4.2±2.4-fold reductions). H_2O_2+CHX and the placebo presented minor changes in Ct values across all time-points assessed (T1:2.1±0.5-fold reduction, T2:1.6±0.2-fold reduction, T3:3.9 ±0.3-fold reduction). CPC+Zn mouthwash and CHX led to a significant reduction in the SARS-CoV-2 viral load in saliva up to 60 min, whereas H_2O_2 provided a significant reduction up to 30 min after rinsing.

Publication	Study design	Setting	Number of included participants	Assessment of viral load	Product, duration of rinse	Comparison	Results
Lamas, *et al*. [22]	Uncontrolled before-after study	Hospitalized and home-isolated patients with positive RT-PCR for SARS-CoV-2 in nasopharyngeal exudate with a median age of 63.5 years. Single rinse performed in a single day.	4	Nasopharyngeal swab and saliva (method not explained), via RT-PCR	PVP-I (1%), 60s	-	In 2 out of 4 patients, PVP-I resulted in a significant drop (~5 $\log_{10}$ and ~2 $\log_{10}$ reductions in salivary viral load in each patient) which remained for at least 3h.
Gottsauner, *et al*. [19]	Uncontrolled before-after study	Hospitalized patients with a positive test for SARS-CoV-2 within the last 72 h with a median age of 55 years. Single rinse performed in a single day.	10	Oropharyngeal swab, via RT-PCR	H_2O_2 (1%), 30s	-	Viral load decrease of 0.3×10^3 copies/mL. No significant differences were observed between the baseline viral load and viral load 30min after the 1% H_2O_2 mouth rinse (p=0.96)
Yoon, *et al*. [20]	Uncontrolled before-after study	Hospitalized patients diagnosed with COVID-19 with a median age of 55.5 years. One rinse per day on two non-consecutive days (Day 3 and 6 of the study)	2	Saliva (method not specified), via RT-PCR	CHX (0.12%), 30s	-	The viral load in the saliva decreased transiently for 2h after using the CHX mouthwash, but it increased again at 2-4h post-mouthwash. On day 3, viral load was not detected at 1h and 2h post rinse, on both patients. One of the patients showed a baseline viral load of 6.9 $\log_{10}$ and the other of 4.9 $\log_{10}$. On day 6, one hour after using the mouthwash, there was no reduction in viral load in one patient.
Schürmann, *et al*. [23]	Uncontrolled before-after study	Hospitalized patients diagnosed with COVID-19. Single rinse performed in a single day.	34	Pharyngeal swab, via RT-qPCR	Linola® sept (analogous composition to Biorepair® Zahnmilch: aqua, sorbitol, xylitol, zinc hydroxyapatite, cellulose gum, zinc PCA, aroma, peg-40, hydrogenated castor oil, sodium lauryl sulfate, sodium myristoyl sarcosinate, sodium methyl, cocoyl taurate, lactoferrin, sodium hyaluronate, sodium saccharin, sodium benzoate, phenoxyethanol, benzyl alcohol), 60s	-	The mean of Ct-values before rinsing was 26.0±5.8. The overall mean of Ct-values after rinsing was 29.1±6.1. Mean values showed an increase of the Ct-values of 3.1±3.6, which translated into a significant reduction of the viral load in the pharynx of about 90%. Most patients exhibited a ten-fold reduction of viral load, independently of the initial viral load. The viral load required approximately six hours to recover to the initial viral load. Moreover, highly infectious patients were able to restore their initial viral load during this time, while less infectious patients were not able

Publication	Study design	Setting	Number of included participants	Assessment of viral load	Product, duration of rinse	Comparison	Results
							to restore their initial infectivity 6h after gargling.
***Jayaraman, *et al*.** [25]	Uncontrolled before-after study	Hospitalized patients diagnosed with COVID-19. Single rinse performed in a single day.	36	Saliva (Passive drool) and Exhaled respiratory droplets, via RT-PCR	PVP-I (1%); H_2O_2 (1.5%); CHX (0.2%). Duration of the rinse not available	-	The reduction was significantly higher in respiratory droplets (92%) than in whole saliva samples (50%; p=0.008). PVP-I: -Saliva 20min: 1.8±1.1 log_{10} reduction 60min: 1.3±0.9 log_{10} reduction - Respiratory droplets 20min: 2.5±0.4 log_{10} reduction 60min: 1.6±1.9 log_{10} reduction H_2O_2: -Saliva 20min: 1.2±0.3 log_{10} reduction 60min: 1.6±1.6 log_{10} reduction 90min: 1.5±1.5 log_{10} reduction 180min: 0.9±0.8 log_{10} reduction -Respiratory droplets 20min: 3.5±3.7 log_{10} reduction 60min: 2.5±2.8 log_{10} reduction 90min: 1.9±1.6 log_{10} reduction 180min: 3.0±0.03 log_{10} reduction CHX -Saliva 90min: 1.6±1.2 log_{10} reduction 180min: 0.4±1.5 log_{10} reduction -Respiratory droplets 90min: 1.2±0.8 log_{10} reduction 180min: 0.6±1.7 log_{10} reduction

CHX: Chlorhexidine Gluconate; **CPC:** Cetylpyridinium Chloride; **Ct:** Cycle threshold; **h:** hours; **H_2O_2:** Hydrogen Peroxide; **log**: logarithm; **min:** minutes; **PVP-I:** Povidone-iodine; **RCT:** Randomized Controlled Trial; **RT-PCR:** Reverse Transcription Polymerase Chain Reaction; **s**: seconds;

Appendix Table 4: *In vitro* efficacy of different mouthwashes on SARS-CoV-2 viral load.

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
A. Povidone-iodine (PVP-I)						
Bidra, *et al*. [29]	USA-WA1/2020; Vero 76	PVP-I (0.5%, 1.25%, 1.5%)	Water; Ethanol (70%)	Clean	15s 30s	15s: >4.3 log_{10} reduction of the infectious virus for all concentrations 30s: >3.6 log_{10} reduction of the infectious virus for all concentrations
Xu, *et al*. [30]	USA-WA1/2020; HEK293T, HeLa	PVP-I (10%) at different final dilutions: 5%, 0.5%, and 0.05%	-	No information available	30min	Only the 5% dilution of PVP-I was effective in inactivating the viruses (0 RLU)
Pelletier, *et al*. [31]	USA-WA1/2020; Vero 76	Oral Rinse PVP-I antiseptic (0.5%, 0.75%, 1.5%)[(i)]	Water; Ethanol (70%)	Clean	60s	After incubation with each nasal/oral antiseptic, viral load decrease of >4 log_{10} infectious viruses for all concentrations
Frank, *et al*. [32]	USA-WA1/2020; Vero 76	PVP-I (0.5%, 1.25%, 2.5%)	Water; Ethanol (70%)	Clean	15s 30s	15s: the solutions tested were effective at reducing the viral load >3 log_{10} for all concentrations 30s: the solutions were effective at reducing the viral load >3.3 log_{10} for all concentrations
Hassandarvish, *et al*. [55]	SARS-COV-2/MY/UM/6-3, TIDREC; Vero E6	PVP-I (0.5%, 1%)	Water	Clean; Dirty (3.0 g/L BSA + 3 ml/L human erythrocytes)	15s 30s 60s	15s: 1% PVP-I reduced >5 log_{10} viral titers. 0.5% PVP-I reduced >4 log_{10} viral load 30s: 0.5% and 1% PVP-I reduced >5 log_{10} viral titers 60s: 0.5% and 1% PVP-I reduced >5 log_{10} viral titers
Meyers, *et al*. [43]	HCoV 229e; HUH7	Betadine® 5%: PVP-I (5%)	-	Dirty (200 µL of 5% BSA)	30s 60s 120s	30s: Decrease in viral load between >3 log_{10} to <4 log_{10} 60s: Decrease in viral load between >3 log_{10} to >4 log_{10} 120s: >4 log_{10} reduction in viral load

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Anderson, *et al*. [44]	hCoV-19/Singapore/2/2020; Vero E6	Antiseptic solution: PVP-I (10%); Antiseptic skin cleanser: PVP-I (7.5%); Gargle and mouthwash: PVP-I (1.0%), 1:2 dilution; Throat spray: PVP-I (0.45%)	PBS	Dirty (0.3 g/L BSA)	30s	≥4 log_{10} reduction of SARS-CoV-2 titers, for all the products.
Bidra, *et al*. [33]	USA-WA1/2020; Vero 76	PVP-I (0.5%, 0.75%, 1.5%)	Water; Ethanol (70%)	Clean	15s 30s	15s: the solutions reduced >3 log_{10} of the viral load 30s: the tested solutions reduced >3.3 log_{10} of the viral load
Meister, *et al*. [45]	BetaCoV/Germany/Ulm/01/2020, BetaCoV/Germany/Ulm/02/2020, UKEssen; Vero E6	Iso-Betadine® mouthwash 1.0%: PVP-I (1%);	Cell culture medium	Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract)	30s	Iso-Betadine® mouthwash reduced viral infectivity to up to 3 log_{10}
***Statkute, *et al*.** [46]	England 2; Vero E6	Videne®: PVP-I (7.5%)	-	Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract	30s	Videne® had an effect of ~3 log_{10} reduction
Davies, *et al*. [49]	England 2; Vero E6	Povident: PVP-I (0.58%)	PBS	Clean	60s	≥4.1 log_{10} reduction or[(ii)] ≥5.2 log_{10} reduction
Jain, *et al*. [39]	SARS-CoV-2 strain used was isolated from a patient; Vero E6	PVP-I (1%)	-	Clean	30s 60s	30s: 99.8% inactivation 60s: >99.9% inactivation

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Kariwa, *et al*. [52]	WK-521; Vero E6	Isodine Gargle (Ethical product) at two different concentations: PVP-I (0.23%) and PVP-I (0.47%) Isodine Gargle (Consumer product): PVP-I (0.23%) Isodine Gargle C (Consumer product): PVP-I (0.35%) Isodine Nodo Fresh (consumer product): PVP-I (0.45%)	-	Clean	30s 60s	Isodine Gargle (Ethical product) PVP-I (0.23%): 30 s: >3.1 log_{10}; 60s: >3.6 log_{10}; Isodine Gargle (Ethical product) PVP-I (0.47%): 30 s: >3.2 log_{10} 60s: >4.0 log_{10}; Isodine Gargle (Consumer product) PVP-I (0.23%): 30 s: >3.1 log_{10}; 60s: >3.6 log_{10}; Isodine Gargle C (Consumer product) PVP-I (0.35%): 30 s: >3.2 log_{10}; 60s: >3.4 log_{10}; Isodine Nodo Fresh (consumer product) PVP-I (0.45%): 30 s: >3.8 log_{10}; 60s: >3.8 log_{10};
Shet, *et al*. [53]	Coronavirus strain OC43, Coronavirus strain NL63, and Coronavirus strain 229E; MRC-5, Vero CCL-81, and HCT-8 cells	PVP-I solution (0.5%, 10%) PVP-I scrub (7.5%) Placebo solution (0.5%) Placebo scrub (7.5%)	Authors did not mention placebo composition.	Clean	<15s 15s 30s 60s 5min	PVP-I (0.5%) solution: **OC43 strain**: 4 log_{10} reduction (<15s); ≥5.75 log_{10} reduction (15s, 30s, 60s, and 5min); **NL63 strain**: 4.75 log_{10} reduction (<15s); ≥5.25 log_{10} reduction (15s, 30s, 60s, and 5min); **229E strain**: 3.75 log_{10} reduction (<15s); 4.25 log_{10} reduction (15s); ≥5.25 log_{10} reduction for contact times of 15s, 30s, 60s, and 5min; PVP-I 7.5% scrub: **OC43 strain**: 2.5 log_{10} reduction (<15s); 3 log_{10} reduction (15s); 3.75 log_{10} reduction (30s, 60s, and 5min); **NL63 strain**: 3.25 log_{10} reduction (<15s, 15s, 30s, 60s, and 5min); **229E strain**: 3.50 log_{10} reduction (<15s, 15s, 30s, 60s, and 5min);

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
						PVP-I 10% solution: **OC43 strain**: 4.50 log_{10} reduction (<15s); ≥5.75 log_{10} reduction (15s, 30s, 60s, and 5min); **NL63 strain**: ≥5.25 log_{10} reduction (<15s, 15s, 30s, 60s, and 5min); **229E strain**: 4 log_{10} reduction (<15s); 4.25 log_{10} reduction (15s); 4.50 log_{10} reduction (30s, 60s, and 5min); Placebo 0.5%: **OC43 strain**: 0.25 log_{10} reduction (<15s); 0.50 log_{10} reduction (15s and 60s); 0.75 log_{10} reduction (30s); 1.25 log_{10} reduction (5min); **NL63 strain**: 0.25 log_{10} reduction (<15s, 15s); 0.50 log_{10} reduction (60s, and 5min); no reduction at 30s **229E strain**: 0.25 log_{10} reduction (<15s); 0.75 log_{10} reduction (30s, 60s, and 5min); 1 log_{10} reduction (15s) Placebo 7.5%: **OC43 strain**: 1.25 log_{10} reduction (<15s, 15 s); 1.75 log_{10} reduction (30s); 3.75 log_{10} reduction (60s, 5min); **NL63 strain**: 1.25 log_{10} reduction (<15s) 1.75 log_{10} reduction (15s); 2 log_{10} reduction (30s); 3.25 log_{10} reduction (60s, 5min); **229E strain**: 1.5 log_{10} reduction (<15s); 1 log_{10} reduction (15s); 2 log_{10}

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
						reduction (30s); 3.25 log_{10} reduction (60s), 3.5 log_{10} reduction (5min)
B. Hydrogen Peroxide (H_2O_2)						
Bidra, *et al*. [29]	USA-WA1/2020; Vero 76	H_2O_2 (1.5%, 3%)	Water; Ethanol (70%)	Clean	15s 30s	15s: H_2O_2 (1.5%) reduced 1.3 log_{10} infectious virus. H_2O_2 (3%) reduced 1.0 log_{10} infectious virus 30s: H_2O_2 (1.5%) reduced 1.0 log_{10} infectious virus. H_2O_2 (3%) reduced 1.8 log_{10} infectious virus
Xu, *et al*. [30]	USA-WA1/2020; HEK293T, HeLa	Colgate® Peroxyl®: H_2O_2 (1.5%) at different dilutions: 0.75%, 0.075%, and 0.0075%	-	No information available	30min	Colgate® Peroxyl® (0.75% and 0.075%) were effective in inactivating the viruses (0 RLU)
Meyers, *et al*. [43]	HCoV 229e; HUH7	Peroxide Sore Mouth Cleanser®: H_2O_2 (1.5%); H_2O_2 solution diluted to 1.5% in PBS: H_2O_2 (1.5%); Orajel™ Antiseptic Rinse: H_2O_2 (1.5%); menthol (0.1%)	-	Dirty (200 µL of 5% BSA)	30s 60s 120s	Virus load reduction between <1 log_{10} to 2 log_{10} for all concentrations and contact times
Meister, *et al*. [45]	BetaCoV/Germany/Ulm/01/2020, BetaCoV/Germany/Ulm/02/2020, UKEssen; Vero E6	Cavex oral rinse: H_2O_2 (concentration unkown)	Cell culture medium	Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract)	30s	Viral load decrease between 0.3 log_{10} and 1.8 log_{10}
Davies, *et al*. [49]	England 2; Vero E6	Peroxyl®: H_2O_2 (1.5%)	PBS	Clean	60s	Reduction of the virus titer by 0.2 log_{10}

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Koch-Heier, *et al*. [50]	SARS-CoV-2 Isolate "FI-100"; Vero E6	H_2O_2 (1.5%)	nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing infection medium and test solution	Clean	30s	H_2O_2 (1.5%) showed no effective reduction of the virus titer
C. Chlorhexidine Gluconate (CHX)						
Xu, *et al*. [30]	USA-WA1/2020; HEK293T, HeLa	CHX (0.12%) used in different final dilutions: 0.06%, 0.006%, and 0.0006%	-	No information available	30min	CHX (0.06%) was effective in inactivating the viruses (0 RLU). CHX (0.006%) had a moderate anti-viral effect (>2x10^4 RLU)
Meister, *et al*. [45]	BetaCoV/Germany/Ulm/01/2020, BetaCoV/Germany/Ulm/02/2020, UKEssen; Vero E6	Chlorhexamed® Forte: CHX (concentration unknown); Dynexidin® Forte 0.2%: CHX (0.2%)	Cell culture medium	Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract)	30s	Viral load decrease between 0.3 $\log_{10}$ and 1.8 $\log_{10}$
Steinhauer, *et al*. [42]	No available information	CHX: 0.1% and 0.2% (used in different dilutions – 0.08% and 0.16%)	Formaldehyde	Clean	15s 30s 60s 5min 10min	Both formulations had >1 $\log_{10}$ reduction of the viral load after 60 s and 5 min (CHX 0.2%) and after 10 min (CHX 0.1%)
Davies, *et al*. [49]	England 2; Vero E6	CHX Antiseptic Mouthwash: CHX (0.2%); Corsodyl (Alcohol Free Mint Flavour): CHX (0.2%)	PBS	Clean	60s	CHX Antiseptic Mouthwash: 0.5 $\log_{10}$ reduction Corsodyl: 0.4 $\log_{10}$ reduction
Jain, *et al*. [39]	SARS-CoV-2 strain used was isolated from a patient; Vero E6	CHX (0.12%) and CHX (0.2%)	-	Clean	30s 60s	For 30 and 60s: CHX (0.12%) led to a 99.9% inactivation. CHX (0.2%) led to a >99.9% inactivation
Koch-Heier, *et al*. [50]	SARS-CoV-2 Isolate "FI-100"; Vero E6	CHX (0.1%)	nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing infection medium and test solution	Clean	30s	CHX (0.1%) showed no effective reduction of the virus titer

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Komine, *et al*. [54]	JPN/TY/WK-521 strain; VeroE6/TMPRSS2	GUM® PAROEX: CHX (0.12%)	PBS Ethanol (70%)	Clean	30s	GUM® PAROEX (0.12%) led to a 0.2 log_{10} reduction
Tiong, *et al*. [40]	SARS-CoV-2 strain used was isolated from a patient, SARS-COV-2/MY/UM/6-3 TIDREC (virus stock); Vero E6	Oradex®: CHX (0.12%)	Culture cell medium	Clean; Dirty (0.3 g/L BSA + 3 mL/L human erythrocytes)	30s 60s	Reduction of 4 log_{10} for all test times and conditions.
***Anderson, *et al*.** [36]	USA-WA1/2020, Alpha isolate: hCoV-19/England/204820464/2020, Beta isolate: hCoV-19/South Africa/KRISP-EC-K005321, and Gamma isolate: hCoV-19/Japan/TY7-503/2021; Vero E6	CHX (0.2%), with flavour	Ethanol (70%)	Clean; Dirty (human saliva)	30s	USA-WA1/2020: CHX (0.2%) led to a 1.26 log_{10} reduction; Alpha isolate: 3.11 log_{10} reduction; Beta isolate: 4.11 log_{10} reduction; Gamma isolate: 3.36 log_{10} reduction
D. Cetylpyridinium Chloride (CPC)						
Meyers, *et al*. [43]	HCoV 229e; HUH7	Crest® Pro-Health™: CPC (0.07%)	-	Dirty (200 µL of 5% BSA)	30s 60s 120s	Crest® Pro-Health™ decreased viral load by at least 3 log_{10} to >4 log_{10} for all contact times
***Statkute, *et al*.** [46]	England 2; Vero E6	Dentyl® Dual Action: CPC (0.05%-0.1%), Other active ingredients: isopropyl myristate, Mentha Arvensis extract; Dentyl® Fresh Protect: CPC (0.05%-0.1%), Other active ingredients: xylitol;	-	Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract	30s	Dentyl® mouthwashes completely eliminated the virus (>5 log_{10} reductions)
***Muñoz-Basagoiti, *et al*.** [38]	SARS-CoV-2 isolated from a nasopharyngeal swab; Vero E6	Vitis® CPC Protec: 2.063 mM of CPC; CPC: 10 mM of CPC diluted in distilled water	Culture cell media	Clean	120s	Viral load decreased by 3 log_{10} for all test solutions
***Green, *et al*.** [48]	HCoV-SARS 229E; MRC-5	Mouthwash containing CPC (0.07%), sodium fluoride, and flavor oil;	-	Clean	30s 60s	Viral load decrease of 3.1 log_{10} for all contact times
Koch-Heier, *et al*. [50]	SARS-CoV-2 Isolate “FI-100”; Vero E6	CPC (0.05%)	nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing	Clean	30s	CPC (0.05%) reduced virus titer by 5.6×10^6 pfu/mL (0.7 log_{10})

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
			infection medium and test solution			
Muñoz-Basagoiti, *et al*. [56]	SARS-CoV-2 D614G (isolated from a nasopharyngeal swab) and SARS-CoV-2 B.1.1.7.; Vero E6	Vitis Encias (1.47 mM of CPC) (or 0.05%); Vitis CPC Protect (with 2.063 mM of CPC) (or 0.07%); CPC (10 mM)	Vehicles containing the same formulation but without CPC; Virus mixed with 1 mL of media as positive control	Clean Dirty (Saliva)	30s 60s 120s	30s: Vitis CPC decreased 10 fold (1 log_{10}) the TCID50/mL of the B.1.1.7 SARS-CoV-2 variant (compared to untreated virus) 60s: There was a reduction of infectivity above 1,000 (>3 log_{10}) times regardless of the variant employed or the duration of exposure to Vitis CPC 120s: High doses of CPC (10 mM) effectively suppressed viral infection. CPC-containing mouthwashes decreased about 1,000 times the TCID50/ml of SARS-CoV-2, while vehicles had no impact on SARS-CoV-2 infectivity when compared to untreated virus

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Komine, *et al*. [54]	JPN/TY/WK-521 strain; VeroE6/TMPRSS2	GUM® WELL PLUS Dental paste: CPC (0.0125%); GUM® MOUTHWASH HERB 2020: CPC (0.04%); GUM® WELL PLUS Dental rinse (alcoholic type): CPC (0.05%); GUM® WELLPLUS Dental rinse (non-alcoholic type): CPC (0.05%); GUM® Oral Rinse: CPC (0.075%); GUM® Disinfection spray for mouth/throat: CPC (0.3%)	PBS Ethanol (70%)	Clean	20s 30s 3min (dental paste)	20s: GUM® MOUTHWASH HERB 2020 (0.04%) led to >4.4 log_{10} reduction; Dental rinse (alcoholic type) (0.05%) led to a 4.2 log_{10} reduction, while GUM® WELLPLUS Dental rinse (non-alcoholic type) (0.05%) led to a 4.1 log_{10} reduction. GUM® Disinfection spray for mouth/throat (0.3%) achieved a >3.4 log_{10} reduction. 30s: GUM® Oral Rinse (0.075%) led to a >4.3 log_{10} reduction 3min: GUM® WELL PLUS Dental paste (0.0125%) led to a 3.3 log_{10} reduction
***Anderson, *et al*.** [36]	USA-WA1/2020, Alpha isolate: hCoV-19/England/204820464/2020, Beta isolate: hCoV-19/South Africa/KRISP-EC-K005321, and Gamma isolate: hCoV-19/Japan/TY7-503/2021; Vero E6	CPC (0.07%), with flavour and mix of herbal extracts; CPC (0.07%), with flavour.	Ethanol (70%)	Clean; Dirty (human saliva)	30s	USA-WA1/2020: both CPC mouthwashes led to a ≥4 log_{10} reduction Alpha isolate: both mouthwashes led to a 3.11 log_{10} reduction; Beta isolate: both mouthwashes led to a 4.11 log_{10} reduction; Gamma isolate: both mouthwashes led to a 3.36 log_{10} reduction
E. Other mouthwashes						
Xu, *et al*. [30]	USA-WA1/2020; HEK293T, HeLa	Listerine® Antiseptic Original: Ethanol (20-30%), Thymol 0.064%, Methyl salicylate 0.06%, Menthol (Racementhol) 0.042%, Eucalyptol 0.092% - (50%, 5%, and 0.5% of the original solutions)	-	No information available	30min	50% dilution of Listerine® Antiseptic was effective in inactivating the viruses (0 RLU) Treatment with 5% Listerine® had a moderate anti-viral effect (>2x10^4 RLU)

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Meyers, *et al*. [43]	HCoV 229e; HUH7	Listerine® Antiseptic: Eucalyptol (0.092%), Menthol (0.042%), Methyl Salicylate (0.06%), Thymol (0.064%); Listerine® Ultra: Eucalyptol (0.092%), Menthol (0.042%), Methyl Salicylate (0.06%), Thymol (0.064%); Equate™: Eucalyptol (0.092%), Menthol (0.042%), Methyl Salicylate (0.06%), Thymol (0.064%); Antiseptic Mouthwash (CVS): Eucalyptol (0.092%), Menthol (0.042%), Methyl Salicylate (0.06%), Thymol (0.064%)	-	Dirty (200 µL of 5% BSA)	30s 60s 120s	Listerine® Antiseptic decreased viral load by >4 log_{10}. After incubation times of 60s and 120s, no remaining infectious virus was detected. Listerine® Ultra, Equate™, and Antiseptic Mouthwash showed lower efficacy, (particularly after 30s). However, these latter mouthwashes decreased infectious virus titers by >2 log_{10}
Meister, *et al*. [45]	BetaCoV/Germany/Ulm/01/2020, BetaCoV/Germany/Ulm/02/2020, UKEssen; Vero E6	Dequonal®: Dequalinium chloride, benzalkonium chloride; Listerine® Cool Mint®: Ethanol, essential oils; Octenident® mouthwash: Octenidine dihydrochloride; ProntOral® mouthwash: Polyaminopropyl biguanide (polyhexanide)	Cell culture medium	Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract)	30s	Dequonal® and Listerine® Cool Mint® significantly reduced viral infectivity to up to 3 log_{10}. Octenident® virucidal activities could be observed with reduction factors ranging between 0.3 log_{10} to 1.8 log_{10}; With ProntOral®, one strain was only moderately reduced and the other 2 strains were inactivated
***Statkute, *et al*.** [46]	England 2; Vero E6	Corsodyl: ethanol (7 %), CHX (0.2%), Other active ingredients: peppermint oil; Listerine® Cool Mint®: ethanol (21%), Other active ingredients: thymol (0.064%), eucalyptol (0.092%), methyl salicylate (0.060%) and menthol (0.042 %); Listerine® Advanced Gum Treatment: ethanol (23 %), Other active ingredients: ethyl lauroyl arginate HCl (0.147%); SCD Max: CPC (0.07-0.1%), sodium citric acid (0.05%), Other active ingredients: sodium monofluorophosphate;	-	Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract	30s	Listerine® Advanced Gum Treatment eliminated the virus (>5 log_{10} reduction). SCD Max and Listerine® Cool Mint® had a moderate effect (~3 log_{10} reduction). Corsodyl was relatively ineffective (<2 log_{10} reduction)
Steinhauer, *et al*. [42]	No available information	octenisept®: octenidine dihydrochloride 0.1%, and phenoxyethanol 20% (used in 20% (v/v) and 80% (v/v) concentration)	Formaldehyde	Clean	15s 30s 60s	Reduction of titers by ≥4.4 log_{10} was observed for both concentrations and all contact times

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Davies, *et al*. [49]	England 2; Vero E6	Listerine® Advanced Defence Sensitive: dipotassium oxalate (1.4%); Listerine® Total Care: Eucalyptol, thymol, menthol, sodium fluoride, zinc fluoride; OraWize+ Aqualution Systems stabilized hypochlorous acid (0.01-0.02%)	PBS	Clean	60s	Listerine® Advanced Defence Sensitive: ≥3.5 log_{10} or[(ii)] ≥4.2 $log_{10;}$ Listerine® Total Care: ≥4.1 log_{10} reduction or[(ii)] ≥5.2 log_{10} OraWize+: ≥5.5 log_{10} or[(ii)] 0.4 log_{10}
***Muñoz-Basagoiti, *et al*.** [38]	SARS-CoV-2 isolated from a nasopharyngeal swab; Vero E6	Perio Aid® Intensive Care: 1.47 mM of CPC and 1.33 mM of CHX	Culture cell media	Clean	120s	No impact on SARS-CoV-2 infectivity, when compared to untreated virus
***Mantlo, *et al*.** [34]	USA-WA1/2020; Vero Cells	CupriDyne®: iodine and cuprous iodide (250 ppm, 25 ppm, 2.5 ppm)	Water (boiling and at room temperature)	Clean	10min 30min 60min	CupriDyne® (25 ppm or 2.5 ppm) were not found to cause a significant difference in SARS-CoV-2 titers; CupriDyne® (250 ppm) was shown to effectively inactivate the virus to a significant extent after 10, 30, and 60min; After incubation with undiluted (250 ppm) CupriDyne® for 10min, viral titers dropped by 1 $log_{10.}$ Viral titers dropped 2 log_{10} after incubation with undiluted CupriDyne® for 30min. Further incubation with undiluted CupriDyne® for 60min reduced viral titers below the limit of detection
***Green, *et al*.** [34]	HCoV-SARS 229E; MRC-5	Mouthwash containing ethanol (15.7%), sodium fluoride, and flavor oil. Mouthwash containing zinc sulfate heptahydrate (0.2%), sodium fluoride, and flavor oil. Mouthwash containing a mix of Amyloglucosidase, Glucose Oxidase, Lysozyme, Colostrum, Lactoferrin, Lactoperoxidase, sodium fluoride, and flavor oil.	-	Clean	30s 60s	Contact with ethanol, zinc, and enzyme, and protein mouthwashes did not provide a substantial reduction in viral counts. Zinc: after 30s reduction of 1.2±0.4 log_{10}, after 60s reduction of 1.8±0.1) log_{10}; Enzymes and proteins: after 30s reduction of 0.3±0.3 log_{10}, after 60s reduction of 0.3±0.3 log_{10}; Ethanol: after 30s reduction of

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
						0.2±0.3 log_{10}, after 60s reduction of 0.3±0.3 log_{10}
Zoltán [35]	USA-WA1/2020; Vero 76	200 µg elemental iodine/mL at three dilutions (1:1; 2:1, and 3:1)	Water; Ethanol (70%)	Clean	60s 90s	60s: 3:1 dilution reduced viral titer by 2 log_{10}, while 2:1 dilution reduced viral titers by 1.7 log_{10} 90s: 1:1 dilution reduced viral titer by 2 log_{10}
Koch-Heier, *et al*. [50]	SARS-CoV-2 Isolate "FI-100"; Vero E6	ViruProX®: (0.05% CPC and 1.5% H_2O_2); BacterX® pro: (0.1% CHX, 0.05% CPC, and 0.005% F-); Solution of CPC (0.05%) and CHX (0.1%)	nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing infection medium and test solution	Clean	30s	Incubation with ViruProX® reduced the virus titer by ≥6.8 × 10^6 pfu/mL (≥1.9 log_{10}) versus the medium control, while BacterX® pro reduced by ≥8.4 × 10^6 pfu/mL (≥2.0 log_{10}) CHX (0.1%) and CPC (0.05%) reduced the virus titer by 6.7×10^6 pfu/mL (1.2 log_{10})
Almanza-Reyes, *et al*. [51]	SARS-CoV-2 NL/2020 (BetaCoV/Netherlands/01); Vero E6	Argovit® silver nanoparticles (0.0004% to 0.5%)	Culture cell media	Clean	72h	Argovit® (0.3%) led to a 80% viral inactivation
Muñoz-Basagoiti, *et al*. [56]	SARS-CoV-2 D614G (isolated from a nasopharyngeal swab) and SARS-CoV-2 B.1.1.7.; Vero E6	Perio Aid Intensive Care (1.47 mM of CPC and 1.33 mM of Chlorhexidine)	Vehicles containing the same formulation but without CPC; Virus mixed with 1 mL of media as the positive control	Clean Dirty (Saliva)	30s 60s 120s	120s: High doses of CPC (10 mM) effectively suppressed viral infection. CPC-containing mouthwashes decreased about 1,000 times the TCID50/ml of SARS-CoV-2, while vehicles had no impact on SARS-CoV-2 infectivity when compared to untreated virus
Santos, *et al*. [57]	SARS.CoV2/SP02.2020.HIAE. Br; Vero CCL-81	Anionic iron tetracarboxyphthalocyanine derivative (APD): 1 mg/mL (1:2), 0.5 mg/mL (1:4), 0.25 mg/mL (1:8), 0.125 mg/mL (1:16), 0.0625 mg/mL (1:32), 0.03125 mg/mL (1:64), 0.01562 mg/mL (1:128)	-	No information available	30 min	Significant reduction in viral load when compared to the positive control at the 1:2 (99.96%, <4 log_{10}), 1:4 (99.88%, <3 log_{10}), 1:8 (99.84%, <3 log_{10}) and 1:16 (92.65%, <2 log_{10}) titers. Minor viral neutralization was

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
						observed at the 1:32 (77.42%) and 1:64 (11.06%) titers. No virus neutralization was observed below the 1:128 titer.
Santos, *et al*. [41]	SARS-CoV-2 strain used was isolated from a patient; Vero ATCC CCL-81	Dental Gel: APD (1%) Mouthwash: APD (0.1%)	Viral solution+cellular system as positive control. Cellular system only as the negative control	Clean	30s 60s 5min	Dental Gel APD (1%): 99.99% (4 log10) reduction for all contact times. Mouthwash APD (0.1%): 90% (1 log10) reduction for all contact times.
Komine, *et al*. [54]	JPN/TY/WK-521 strain; VeroE6/TMPRSS2	CPC+CHX Mouthwash: 2 formulations: GUM® PAROEX, CHX (0.06%) + CPC (0.05%); GUM® PAROEX, CHX (0.12%) + CPC(0.05%) GUM® PerioShield: Delmopinol Hydrochloride Mouthwash (0.2%)	PBS Ethanol (70%)	Clean	30s	30s: Both CPC+CHX mouthwash formulations led to a >4.3 log_{10} reduction. The Delmopinol Hydrochloride Mouthwash (0.2%) led to a >5.3 log_{10} reduction.
Shewale, *et al*. [37]	USA-WA1/2020; Vero E6	ClōSYS® Ultra Sensitive rinse, Sensitive rinse, Oral Spray: Stabilized chlorine dioxide (0.1%) ClōSYS® Fluoride toothpaste: Stabilized chlorine dioxide (0.04%)	PBS	Clean	30s 60s 120s	30s: Ultra sensitive rinse led to a 1.96 log_{10} reduction; Sensitive rinse led to a 1.81 log_{10} reduction; Oral Spray led to a 2.98 log_{10} reduction; 60s: Ultra sensitive rinse led to a 1.39 log_{10} reduction; Sensitive rinse led to a 1.71 log_{10} reduction; Oral Spray led to a 2.67 log_{10} reduction; The Sensitive fluoride toothpaste achieved a 2.26 log_{10} reduction with application times of 30s 60s, and 120s.

Publication	SARS-CoV-2 strain(s); Cellular line	Test mouthwashes (concentrations)	Comparison	Interfering substances	Contact time	Results
Meister, *et al*. [47]	SARS-CoV-2 hCoV-19/Germany/BY-Bochum-1/2020; Vero E6	Oral sprays: A) Carragelose® (1.2 mg/mL), Kappa-Carrageenan (0.4 mg/mL), Sodium chlorite; B) Sodium chlorite (0.9%), Panthenol; C) Xylometazolin hydrochloride (1 mg/mL), Dexpanthenol (50 mg/mL); D) Sodium hypochlorite (<0.08%), Lithiummagnesium-sodium-silicate; E) Xylometazolin hydrochloride (0.1%); F)Hydroxypropyl methyl cellulose, Succinic acid, Disodium succinate; G) Galphimia, Luffa operculate, Sabadilla; Nasal sprays: H) Zincum aceticum, Zincum gluconium; I) Anise oil, Eucalyptus oil, Levomenthol, Myrrh extract, Clove oil, Peppermint oil Ratanhia root extract, Tormentil root extract	Cell culture medium	Dirty (substance mimicking nasal secretion)	30s	In general, oral sprays led to a >1 log_{10} reduction: A) 0.53 log_{10} reduction; B) 0.13 log_{10} reduction; C) 0.09 log_{10} reduction; E) 0.20 log_{10} reduction; F) 0.18 log_{10} reduction. Oral spray G) led to no reduction, while oral spray D) led to a 2.21 log_{10} reduction. Nasal spray H) led to no reduction on viral load. Nasal spray I) led to a ≥3.03 log_{10} or ≥ 4.69 log_{10} (large volume plating: to reduce cell toxicity)
Tiong, *et al*. [40]	SARS-CoV-2 strain used was isolated from a patient, SARS-COV-2/MY/UM/6-3 TIDREC (virus stock); Vero E6	Colgate Plax® Fruity Fresh: CPC (0.075%), 0.05% Sodium fluoride; Thymol®: Mouthwash by Xepa 0.05% Thymol Bactidol®: 0.1% Hexetidine, 9% Ethanol Salt water: 2% (0.34 M) Sodium chloride	Culture cell medium	Clean; Dirty (0.3 g/L BSA + 3 mL/L human erythrocytes)	30s 60s	Colgate Plax® Fruity Fresh: 5 log_{10} reduction for all test times and conditions; Thymol® mouthwash by Xepa: 0.75 log_{10} reduction after 60s (clean conditions), 0.5 log_{10} reduction after 30s (clean conditions), and after 30s and 60s (Dirty conditions); Bactidol®: 5 log_{10} reduction for all test times and conditions; Salt water: no effect on SARS-CoV-2 viral load.

*****preprint article; **~** should be read as "approximately"; **APD:** Anionic iron tetracarboxyphthalocyanine; **BSA:** Bovine Serum Albumin; **CHX:** Chlorhexidine Gluconate; **CPC:** Cetylpyridinium Chloride; **F^-:** Fluoride anion; **h:** hours; **H_2O_2:** Hydrogen Peroxide; **(i)**A nasal PVP-I antiseptic (0.5%, 1.25%, 2.5%) was studied as a complement to the oral antiseptic; **(ii)**depending on initial viral concentration (higher, lower); **log:** logarithm; **min:** minutes; **mM:** Millimolar; **PBS:** phosphate buffered saline; **pfu:** Plaque forming units; **ppm:** parts per million; **PVP-I:** Povidone-iodine; **RLU:** Relative Light Units; **s:** seconds;

Database	Query
MEDLINE (via PubMed)	(mouthwash* OR "mouth rinse" OR "oral rinse" OR rinse OR gargl* OR "gargle lavage" OR "oral irrigation" OR "oral lavage") AND (COVID-19 OR COVID19 OR sars-cov-2 OR 2019-nCoV OR COVID OR coronavirus)
Scopus	(mouthwash* OR "mouth rinse" OR "oral rinse" OR rinse OR gargl* OR "gargle lavage" OR "oral irrigation" OR "oral lavage") AND (covid-19 OR covid19 OR sars-cov-2 OR 2019-ncov OR covid OR coronavirus)
Web of Science	TS=((mouthwash* OR "mouth rinse" OR "oral rinse" OR rinse OR gargl* OR "gargle lavage" OR "oral irrigation" OR "oral lavage") AND (COVID-19 OR COVID19 OR sars-cov-2 OR 2019-nCoV OR COVID OR coronavirus))
MedRxiv and bioRxiv	COVID-19 AND mouthwash

PVP-I *in vitro*														
Concentration	**Contact time**	Bidra, *et al.* [29]	Pelletier, *et al.* [31]	Frank, *et al.* [32]	Hassandarvish, *et al.* [55]	Anderson, *et al.* [44]	Bidra, *et al.* [33]	Meister, *et al.* [45]	Meyers, *et al.* [43]	*Statkute, *et al.* [46]	Davies, *et al.* [49]	Jain, *et al.* [39]	Kariwa, *et al.* [52]	Shet, *et al.* [53]
~0.5%[i]	15s	+		±	+		±							+
	30s	±		±	+	+	±						±	+
	60s		+		+						+		± +	+
0.75%	15s						±							
	30s						±							
	60s		+											
1.0%	15s				+									
	30s				+	+		−				−		
	60s				+							±		
1.25%	15s	+		±										
	30s	±		±										
	60s		+											
1.5%	15s	+					±							
	30s	±					±							
	60s		+											
2.5%	15s			±										
	30s			±										
	60s		+											
>2.5%[ii]	15s													± +
	30s					+			±	−				± +

60s							± +					± +

[i]ranging from 0.45% to 0.58%; [ii]concentrations up to 10%; ~ should be read as “approximately”; * preprint article.

Mouthwash	Concentration	Contact time	Bidra, *et al.* [29]	Meyers, *et al.* [43]	Davies, *et al.* [49]	Meister, *et al.* [45]	Steinhauer, *et al.* [42]	*Statkute, *et al.* [46]	*Green, *et al.* [48]	Koch-Heier, *et al.* [50]	Jain, *et al.* [39]	Muñoz-Basagoiti, *et al.* [56]	Komine, *et al.* [54]	Tiong, *et al.* [40]	*Anderson, *et al.* [36]
H_2O_2	1.5%	15s	−												
		30s	−	−						−					
		60s		−	−										
	3%	15s	−												
		30s	−												
CHX	≤0.16%[i]	15s					−								
		30s					−			−	±		−	+	
		60s					−							+	
	0.2%	30s				−					±				− ± +
		60s			−										
CPC	≤0.3%[ii]	20s											± +		
		30s		± +				+	±	−		−	+		
		60s		± +					±			±			

[i]includes concentrations of 0.08%, 0.1%, 0.12%, and 0.16%; [ii]includes concentrations of 0.04%, 0.05%, 0.07%, 0.075%, 0.1%, and 0.3%; * preprint article.

Mouthwash	Contact time	Meyers, *et al.* [43]	Meister, *et al.* [45]	*Statkute, *et al.* [46]	Davies, *et al.* [49]	Steinhauer, *et al.* [42]	*Green, *et al.* [48]	Zoltán [35]	Koch-Heier, *et al.* [50]	Santos, *et al.* [41]	Komine, *et al.* [54]	Shewale, *et al.* [37]	Tiong, *et al.* [40]	Meister, *et al.* [47]
Listerine® Antiseptic	30s	+												
	60s	+												
Listerine® Ultra	30s	−												
	60s	−												
Listerine® Cool Mint®	30s		−	−										
Listerine® Advanced Gum Treatment	30s			+										
Listerine® Advanced Defence Sensitive	60s				± +									
Listerine® Total Care	60s				+									
Equate™	30s	−												
	60s	−												
Antiseptic Mouthwash (CVS)	30s	−												
	60s	−												
Dequonal®	30s		−											
Octenident®	30s		−											
ProntOral®	30s		−											
Corsodyl	30s			−										
SCD Max	30s			−										
octenisept®	15s					+								

	30s					⊕								
	60s					⊕								
OraWize+	60s				⊖ ⊕									
Mouthwash containing ethanol (15.7%), other ingredients	30s						⊖							
	60s						⊖							
Mouthwash containing zinc sulfate heptahydrate, other ingredients	30s						⊖							
	60s						⊖							
Mouthwash containing a mix of Amyloglucosidase, other ingredients	30s						⊖							
	60s						⊖							
Essential iodine solution	60s							⊖						
ViruProx®	30s								⊖					
BacterX® pro	30s								⊖					
Solution ofCPC (0.05%)+CHX (0.1%)	30s								⊖					
Dental Gel: APD (1%)	30s									⊕				
	60s									⊕				
Mouthwash: APD (0.1%)	30s									⊖				
	60s									⊖				
GUM® PAROEX, CHX (0.06%)+CPC (0.05%); GUM® PAROEX, CHX (0.12%)+CPC(0.05%)	30s										⊕			
GUM® PerioShield	30s										⊕			
ClōSYS® Ultra Sensitive rinse,	30s											⊖		

Sensitive rinse, Oral Spray, Fluoride toothpaste	60s										−		
Colgate Plax® Fruity Fresh	30s											+	
	60s											+	
Thymol®	30s											−	
	60s											−	
Bactidol®	30s											+	
	60s											+	
Salt water (2%)	30s											−	
	60s											−	
Carragelose® (1.2 mg/mL), Kappa-Carrageenan (0.4 mg/mL), Sodium chlorite	30s												−
Sodium chlorite (0.9%), Panthenol	30s												−
Xylometazolin hydrochloride (1 mg/mL), Dexpanthenol (50 mg/mL); D) Sodium hypochlorite (<0.08%), Lithiummagnesium-sodium-silicate	30s												−
Xylometazolin hydrochloride (0.1%)	30s												−
Hydroxypropyl methyl cellulose, Succinic acid, Disodium succinate	30s												−
Galphimia, Luffa operculate, Sabadilla	30s												−
Zincum aceticum, Zincum gluconium	30s												−

Anise oil, Eucalyptus oil, Levomenthol, Myrrh extract, Clove oil, Peppermint oil Ratanhia root extract, Tormentil root extract	30s												± +

* preprint article. NOTE: Appendix Table 4 can be consulted for to assess the ingredients of test solutions.